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MAR 26 1992

THE ROCKEFELLER UNIVERSITY
1230 YORK AVENUE • NEW YORK, NEW YORK 10021-6399

March 25, 1992

Dear Dr. Lederberg,

I thought that you might be interested in a reprint of my recent work using a defective HSV vector as a gene transfer agent for the adult rat brain. Since you were so instrumental in discovery and characterization of the bacterial lacZ gene, I thought that you would be particularly interested in our use of this gene as a reporter for our initial trials. Although I only mention it briefly in the paper, I actually spent considerable time working out conditions to specifically detect expression of the bacterial gene and to completely eliminate endogenous, lysosomal β-galactosidase like activity in the rat brain. As a result, I became quite familiar with the literature on β-galactosidase enzymology. Since other groups using different viral vectors are also using lacZ as a reporter, specific staining has become quite controversial, since many groups use conditions which we have found do not prevent endogenous enzyme activity. As a result, I have quite inadvertently become considered as an authority on lacZ activity in the brain, with several groups throughout the country calling to discuss our staining technique and the problem of endogenous enzymatic activity in general. Given your history with this gene, I thought that you might find this to be amusing. *

Currently, I am using lacZ as a reporter for studying regulation of neuronal promoters in the living brain. Since most promoter studies are performed in tissue culture, we feel that the defective HSV vectors will provide a very powerful tool for applying similar principles to analysis of gene expression in the intact, functioning brain. In this way, we can take ordinary plasmids with chimeric promoter-lacZ expression units, turn them into virus, infect the rat brain and then assay for expression both in terms of cell number (through X-gal staining) and through quantitation of lacZ mRNA expression (through in situ hybridization), under various physiologic conditions. If you ever have any suggestions on my work which you feel might be helpful, or if you would simply like to discuss my science in general, I would be delighted to hear from you.

My father sends his best wishes and looks forward to visiting you and your laboratory soon.

That would be good.

Sincerely,

Michael Kaplitt

Michael Kaplitt

* what do you think of Matsuoka et al., Science 10/4/91?